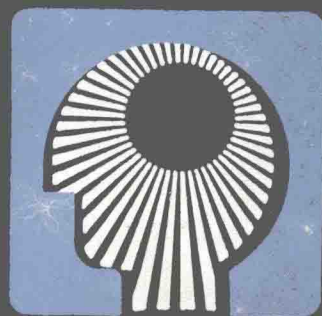


CNS Complications of Malignant Disease

Edited by
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CNS COMPLICATIONS OF MALIGNANT DISEASE

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**CNS COMPLICATIONS
OF
MALIGNANT DISEASE**

Foreword

New developments in treatment have greatly influenced the ultimate course of many malignant tumours. Some of the most substantial improvements in prognosis have been in the acute leukaemias and in the lymphomas. The natural history of one of these conditions, namely acute lymphoblastic leukaemia, was so modified by chemotherapy that central nervous system infiltration, which previously had been only rarely recorded, became one of the commonest and most serious complications. As therapeutic interest has focused on this problem, so there has grown an awareness of the importance of the central nervous system (CNS) as a sanctuary site in this and other neoplasms. The very real difficulties of assessing and treating malignant disease in the CNS led to the organisation of an international symposium in 1978 in Southampton, England to collect the clinical and experimental data from scientists and clinical specialists of various disciplines.

The range of their experience reflects the complexities of the problems because although the many associations between malignant disease in its various forms and the CNS are well known, the contrasts between the characteristics of the two cell systems are conspicuous. The behaviour of most proliferating tumour cells which grow and spread, often via lymphatics, is utterly unlike the normal physiology of the CNS where cell turnover is minimal, where there is no lymphatic system and where the whole tissue is uniquely protected by the blood-brain barrier. Tumours can of course arise from any of the cells which comprise the CNS and metastases blood-borne from outside the CNS are common. The former are peculiar in their limited capacity for metastasis but all tumours in the CNS present special difficulties in diagnosis and, because of the blood-brain barrier, in their treatment by cytotoxic drugs.

Many of the problems are epitomised in the diagnosis and treatment of acute lymphoblastic leukaemia (ALL). This is exemplified in Section One, where Dr Price describes the process of meningeal infiltration and two pathological entities attributable to therapy.

This leads to a general consideration of strategy in the prophylaxis and treatment of leukaemia in the CNS in Section Two. (Purists may wish to refer to early pre-symptomatic treatment rather than prophylaxis or prevention.) The benefits of radiation and of methotrexate are limited by their damaging side effects, some of which are considered in detail in Section Six, so that the alternatives propounded by Drs Simone, Clarkson and Sinks need careful comparison. One point which requires emphasis is the long-term effects of these relatively recent treatments, especially the possibility of second tumour formation which can as yet only be surmised but must probably be counted as a debit against radiation-dependent regimens.

The problem of CNS infiltration in acute myelogenous leukaemia (AML) and in blast crisis of chronic myeloid leukaemia is considered but obviously remains of minor importance until better general control of systemic disease can be achieved. In Section Three the incidence of lymphomatous infiltration is assessed. Here again, the value of treatment directed at the CNS is at present small, but must be enhanced if and when more effective general treatment is developed. Section Four outlines a single but important complication of myeloma and indicates the value of energetic treatment of paraplegia in these patients.

Section Five deals with an all too familiar problem, that of cranial metastases from bronchial carcinoma. As with lymphoma the results of trials show that some benefits can be gained from prophylaxis but the major problem still lies outside the CNS.

Sections Six and Seven deal with some of the complications of therapy and show that the margin of safety is narrow. The negative CAT scan data from Bristol will be reassuring and lend some support to the concept that such abnormalities occur only when radiation is combined with relatively large cumulative doses of methotrexate. It is also reassuring that current regimens appear to cause insignificant damage to the hypothalamus and pituitary function but the impairment of intellectual function, documented by Dr Eiser, must be taken as a warning of the need to modify current regimens. The hazard of activating neuroviruses through immunosuppressive treatments is also real, but specific antiviral chemotherapy is now becoming available. In this section also, Dr Webb's wide-ranging review of the role of neuroviruses in relation to malignant disease is a reminder of the scope of possible progress. Section Eight outlines some new approaches to diagnostic technology and defines existing limitations in diagnosis, while Section Nine summarises the scope of surgery and radiotherapy, presenting a detailed review of achievements attributable to radiotherapy and also an indication of the limitations of this technique. Improvements must lie with the possible use of radiation potentiators or as described in Section Ten with new agents, new techniques of administration and a much greater understanding of the pharmacokinetics and interactions of currently available drugs.

None of the discussions has been reproduced in the book, but many of the authors have adapted their texts to cover some of the points which were raised. Although no clear pattern of investigation or management has yet emerged it is to be hoped that the current strong interest in neoplastic infiltration of the CNS demonstrated in this book will provoke additional study and this, in turn, further improvements in prognosis.

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**HISTOPATHOGENESIS OF
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